



## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA-2022-D-0235]

### Clinical Pharmacology Considerations for the Development of Oligonucleotide

### Therapeutics; Draft Guidance for Industry; Availability

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice of availability.

**SUMMARY:** The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Clinical Pharmacology Considerations for the Development of Oligonucleotide Therapeutics.” This draft guidance describes FDA’s recommendations regarding clinical pharmacology considerations during the development of oligonucleotide therapeutics, including characterizing the potential for QT interval prolongation, performing immunogenicity risk assessment, characterizing the impact of hepatic and renal impairment, and assessing the potential for drug-drug interactions. The intent of this guidance is to assist industry in the conduct of these studies.

**DATES:** Submit either electronic or written comments on the draft guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

**ADDRESSES:** You may submit comments on any guidance at any time as follows:

#### *Electronic Submissions*

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your

comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

#### *Written/Paper Submissions*

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

*Instructions:* All submissions received must include the Docket No. FDA-2022-D-0235 for "Clinical Pharmacology Considerations for the Development of Oligonucleotide Therapeutics." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information

you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at:

<https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

*Docket:* For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

**FOR FURTHER INFORMATION CONTACT:** Anuradha Ramamoorthy, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave, Bldg. 51, Rm. 3118, Silver Spring, MD, 20903, [anuradha.ramamoorthy@fda.hhs.gov](mailto:anuradha.ramamoorthy@fda.hhs.gov), 240-402-6426.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

FDA is announcing the availability of a draft guidance for industry entitled “Clinical Pharmacology Considerations for the Development of Oligonucleotide Therapeutics.”

Oligonucleotide therapeutics are an emerging therapeutic modality with increasing numbers of drugs in development. While antisense and siRNA oligonucleotide therapeutics have been approved in recent years to treat rare diseases, many oligonucleotide therapeutics are in development to treat common chronic diseases. This guidance provides recommendations to assist industry in the development of oligonucleotide therapeutics. Specifically, this guidance represents FDA’s recommendations for certain pharmacokinetic and pharmacodynamic investigations including characterizing QT interval prolongation potential, performing immunogenicity risk assessment, characterizing the impact of hepatic and renal impairment, and assessing the potential for drug-drug interactions during oligonucleotide therapeutic development. This guidance provides recommendations on when these assessments may be appropriate and what types of assessments can help address these issues.

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). This draft guidance, when finalized, will represent the current thinking of FDA on “Clinical Pharmacology Considerations for the Development of Oligonucleotide Therapeutics.” It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

**II. Paperwork Reduction Act of 1995**

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR 312 for investigational new drug applications and 21 CFR part 314 for new drug applications and abbreviated new drug applications have been approved under OMB control numbers 0910-0014 and 0910-0001. The collections of information for biologics license applications have been approved under OMB control number 0910-0338.

### III. Electronic Access

Persons with access to the internet may obtain the draft guidance at either <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs> or <https://www.regulations.gov>.

Dated: June 21, 2022.

**Lauren K. Roth,**

*Associate Commissioner for Policy.*